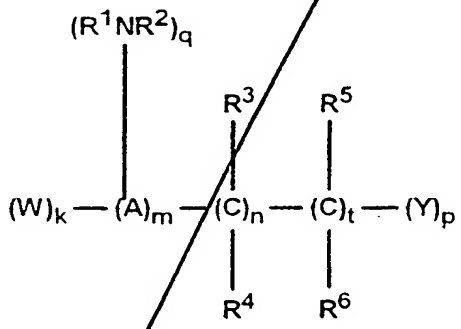
CLAIMS

1. A method for inhibiting IAPP-associated amyloid deposits in a subject, comprising administering to said subject an effective amount of an IAPP fibril inhibiting compound, or a pharmaceutically acceptable salt thereof, such that said IAPP-associated amyloid deposits are inhibited.

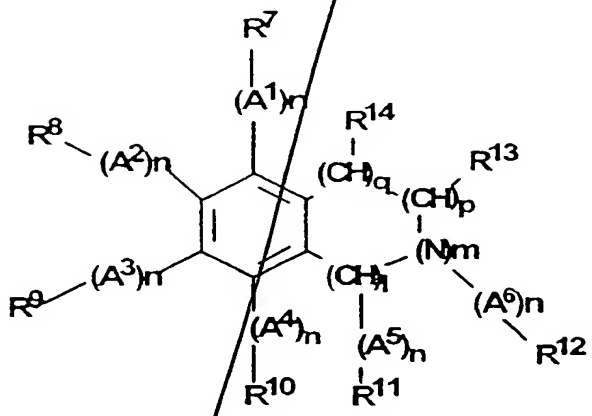
2. The method of claim 1 wherein said IAPP fibril inhibiting compound is of the formula



wherein k, m, t, p and q are independently 0 or 1; n is an integer from 0 to 3; C is a carbon; N is a nitrogen; W is hydrogen or an anionic group at physiological pH; Y is an anionic group at physiological pH; R^1 and R^2 are independently hydrogen, alkyl, an anionic group at physiological pH, or R^1 and R^2, taken together with the nitrogen to which they are attached, may form an unsubstituted or substituted heterocycl having from 3 to 7 atoms in the heterocyclic ring; R^3 is hydrogen, halogen, thiol or hydroxyl; R^4, R^5, and R^6 are independently hydrogen or halogen; and A is hydrogen or C_1 to C_6 alkyl; or a pharmaceutically acceptable ester, acid or salt thereof.

3. The method of claim 2, wherein said IAPP fibril inhibiting compound is selected from the group consisting of 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid; DL-2-amino-5-phosphovaleric acid; 4-Phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine; cyclohexylsulfamic acid; *O*-phospho-*L*-serine; hexafluoroglutaric acid; 8-methoxyquinoline-5-sulfonic acid; 3-amino-2-hydroxy-1-propanesulfonic acid; and 3-dimethylamino-1-propanesulfonic acid, and pharmaceutically acceptable salts thereof.

4. The method of claim 1 wherein said IAPP fibril inhibiting compound is of the formula



wherein C is a carbon; N is a nitrogen; H is a hydrogen; A^1, A^2, A^3, A^4, A^5 and A^6 are independently alkyl, O, S, or -NH; m and n (for each individual A group) are independently 0 or 1; p, q and l are independently 0, 1, or 2; R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, and each R^{14} are independently hydrogen, alkyl, alicyclyl, heterocycyl or aryl, each R^{13} is independently hydrogen, alkyl, alicyclyl. heterocycyl, aryl or an anionic group, and adjacent R groups (e.g., R^7 and R^8) may form an unsubstituted or substituted cyclic or heterocyclic ring.

5. The method of claim 4 wherein said compound is 1,2,3,4-tetrahydroisoquinoline.

6. The method of claim 1, wherein said IAPP fibril inhibiting compound is administered *in vitro* or *ex vivo*.

7. The method of claim 1, wherein said subject has IAPP-associated amyloid deposits in pancreatic islets.

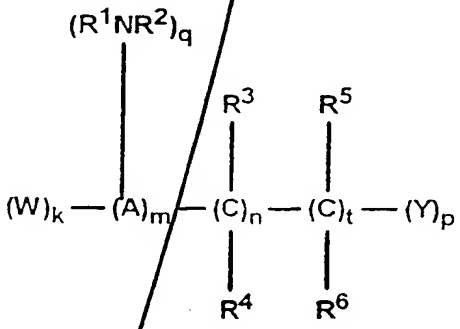
8. A method for inhibiting IAPP fibrillogenesis in a subject, comprising administering to said subject an effective amount of an IAPP fibril inhibiting compound, or a pharmaceutically acceptable salt thereof, such that IAPP fibrillogenesis is inhibited.

9. The method of claim 8, wherein said IAPP fibril inhibiting compound

is administered *in vitro* or ex vivo.

10. A method for reducing IAPP-associated amyloid deposits in a subject having IAPP-associated amyloid deposits, the method comprising administering to said subject an effective amount of an IAPP fibril inhibiting compound, or a pharmaceutically acceptable salt thereof, such that said IAPP-associated amyloid deposits are inhibited.

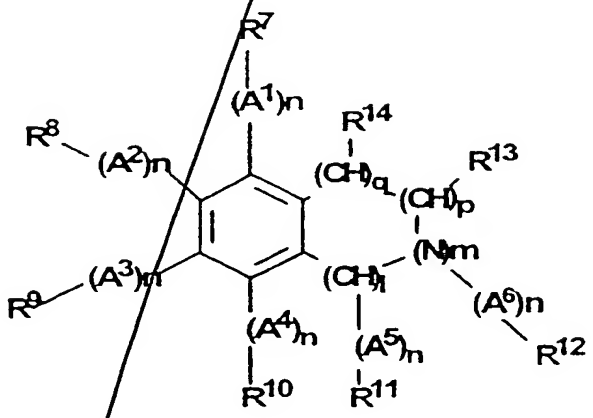
11. The method of claim 10 wherein said IAPP fibril inhibiting compound is of the formula



wherein k, m, t, p and q are independently 0 or 1; n is an integer from 0 to 3; C is a carbon; N is a nitrogen; W is hydrogen or an anionic group at physiological pH; Y is an anionic group at physiological pH; R^1 and R^2 are independently hydrogen, C_1 to C_4 alkyl, an anionic group at physiological pH, or R^1 and R^2, taken together with the nitrogen to which they are attached, may form an unsubstituted or substituted heterocycle having from 3 to 7 atoms in the heterocyclic ring; R^3 is hydrogen, halogen, thiol or hydroxyl; R^4, R^5, and R^6 are independently hydrogen or halogen; and A is hydrogen or C_1 to C_6 alkyl, or a pharmaceutically acceptable ester, acid or salt thereof.

12. The method of claim 11, wherein said IAPP fibril inhibiting compound is selected from the group consisting of 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid; DL-2-amino-5-phosphovaleric acid; 4-Phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine; cyclohexylsulfamic acid; *O*-phospho-*L*-serine; hexafluoroglutaric acid; 8-methoxyquinoline-5-sulfonic acid; 3-amino-2-hydroxy-1-propanesulfonic acid; and 3-dimethylamino-1-propanesulfonic acid, and pharmaceutically acceptable salts thereof.

13. The method of claim 10 wherein said IAPP fibril inhibiting compound is of the formula



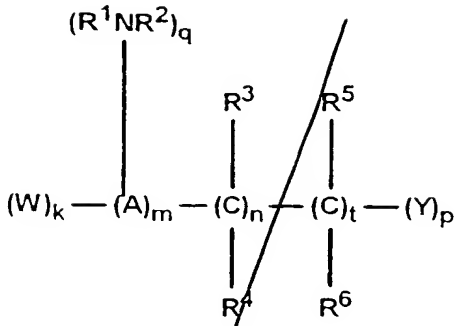
wherein C is a carbon; N is a nitrogen; H is a hydrogen; A^1, A^2, A^3, A^4, A^5 and A^6 are independently alkyl, O, S, or -NH; m and n (for each individual A group) are independently 0 or 1; p, q and l are independently 0, 1, or 2; R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, and each R^{14} are independently hydrogen, alkyl, alicyclyl, heterocycyl or aryl, each R^{13} is independently hydrogen, alkyl, alicyclyl, heterocycyl, aryl or an anionic group, and adjacent R groups (e.g., R^7 and R^8) may form an unsubstituted or substituted cyclic or heterocyclic ring.

14. The method of claim 13 wherein said compound is 1,2,3,4-tetrahydroisoquinoline.

15. The method of claim 10, wherein said IAPP fibril inhibiting compound is administered *in vitro* or *ex vivo*.

16. The method of claim 10, wherein said subject has IAPP-associated amyloid deposits in pancreatic islets.

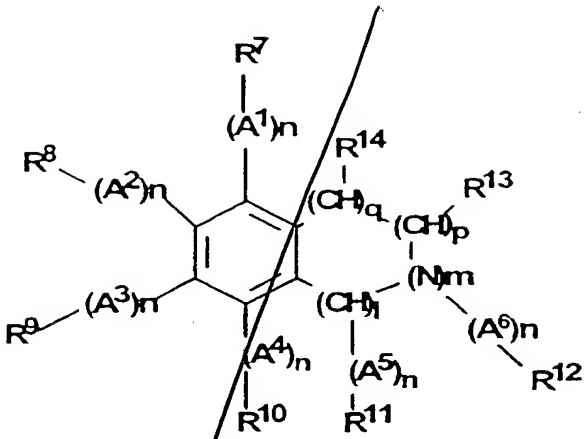
17. A method for inhibiting amyloid deposits in a subject, comprising administering to said subject an effective amount of a compound of the formula



wherein k, m, t, p and q are independently 0 or 1; n is an integer from 0 to 3; C is a carbon; H is a hydrogen; W is hydrogen or an anionic group at physiological pH; Y is an anionic group at physiological pH; R^1 and R^2 are independently hydrogen, C_1 to C_4 alkyl, an anionic group at physiological pH, or R^1 and R^2, taken together with the nitrogen to which they are attached, may form an unsubstituted or substituted heterocycle having from 3 to 7 atoms in the heterocyclic ring; R^3 is hydrogen, halogen, thiol or hydroxyl; R^4, R^5, and R^6 are independently hydrogen or halogen; and A is hydrogen or C_1 to C_6 alkyl; or a pharmaceutically acceptable ester, acid or salt thereof, such that said amyloid deposits are inhibited.

18. The method of claim 17, wherein said IAPP fibril inhibiting compound is selected from the group consisting of 3-(3-hydroxy-1-propyl)amino-1-propanesulfonic acid; DL-2-amino-5-phosphovaleric acid; 4-Phenyl-1-(3'-sulfopropyl)-1,2,3,6-tetrahydropyridine; cyclohexylsulfamic acid; *O*-phospho-*L*-serine; hexafluoroglutaric acid; 8-methoxyquinoline-5-sulfonic acid; 3-amino-2-hydroxy-1-propanesulfonic acid; and 3-dimethylamino-1-propanesulfonic acid, and pharmaceutically acceptable salts thereof.

19. A method for inhibiting amyloid deposits in a subject, comprising administering to said subject an effective amount of a compound of the formula



wherein C is a carbon; N is a nitrogen; H is a hydrogen; A^1, A^2, A^3, A^4, A^5 and A^6 are independently alkyl, O, S, or -NH; m and n (for each individual A group) are independently 0 or 1; p, q and r are independently 0, 1, or 2; R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, and each R^{14} are independently hydrogen, alkyl, alicyclyl, heterocycyl or aryl, each R^{13} is independently hydrogen, alkyl, alicyclyl, heterocycyl, aryl or an anionic group, and adjacent R groups (e.g., R^7 and R^8) may form an unsubstituted or substituted cyclic or heterocyclic ring.

20. The method of claim 19 wherein said compound is 1,2,3,4-tetrahydroisoquinoline.

21. An IAPP fibril inhibiting compound as defined in any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, for use in inhibiting IAPP-associated amyloid deposits in a subject.

22. Process for the preparation of cells suitable for transplantation into a mammal, which cells are capable of forming amyloid deposits, said process comprising contacting the cells *in vitro* with an inhibitor of amyloid deposit formation.

23. Process according to claim 22 wherein said inhibitor causes breakdown of amyloid deposits, the deposits having been formed by said cells prior

to said contacting.

24. Process according to claim 22 or claim 23 in which the cells are cultured in the presence of the inhibitor.

25. Process according to any one of claims 22 to 24 wherein the inhibitor is a compound as defined in claim 2.

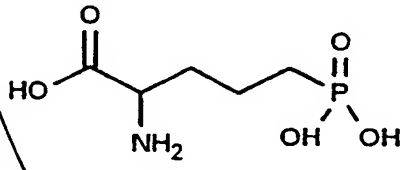
26. Process according to any one of claims 22 to 24 wherein the inhibitor is a compound as defined in claim 4.

27. Process according to any one of claims 22 to 26 wherein the inhibitor is

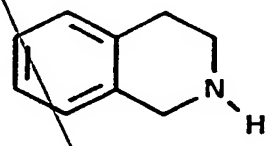
(i) 3-(3-hydroxy-1-propyl) amino-1- propanesulfonic acid

$HOCH_2CH_2CH_2NHCH_2CH_2CH_2SO_3H$,

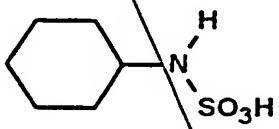
(ii) DL-2-amino-5-phosphovaleric acid



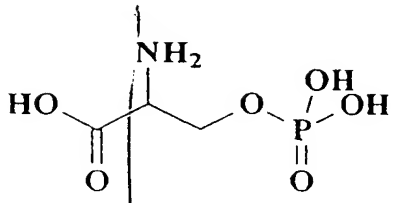
(iii) 1, 2, 3, 4 tetrahydroisoquinoline



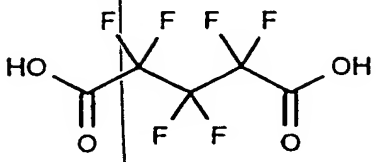
(iv) Cyclohexylsulfamic acid



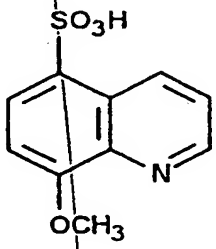
(v) O-Phospho-L-serine



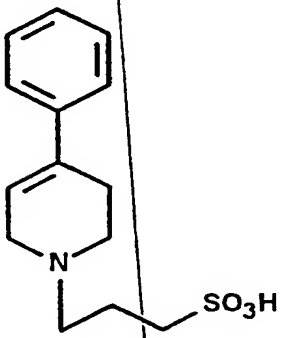
(vi) Hexafluoroglutaric acid



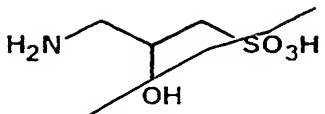
(vii) 8-methoxyquinoline-5-sulfonic acid



(viii) 4-phenyl-1- (3'-sulfopropyl)- 1, 2, 3, 6 - tetrahydropyridine



(ix) 3-amino-2-hydroxy-1- propanesulfonic acid



or

(x) 3-dimethylamino-1-propanesulfonic acid

$Me_2NCH_2CH_2CH_2SO_3H$;

or a salt thereof.

28. Process according to any one of claims 22 to 27 wherein the cells are islet, liver, muscle, kidney, neuronal or stem cells.

29. Process according to any one of claims 22 to 28 wherein the cells are human, primate, rodent, rabbit, ovine, porcine, feline or canine cells.

30. Process according to any one of claims 22 to 29 wherein the amyloid deposits comprise islet amyloid polypeptide, Aβ peptide (involved in Alzheimer's disease), prion protein, immunoglobulin light chain, amyloid A protein, transthyretin, cystatin, β2-microglobulin, apolipoprotein A-1, gelsolin, calcitonin, atrial natriuretic factor, lysozyme variants, insulin, or fibrinogen.

31. Process according to any of claims 22 to 30 wherein the cells are islet cells and the deposits comprise human islet amyloid polypeptide.

32. A culture medium or a ~~culture medium pre-mix which comprises an~~ inhibitor or ~~compound~~ as defined in any one of claims 2, 4, 22 or 27.

33. A culture of cells in which the culture medium is as defined in claim 32.

34. A culture according to claim 33 in which the cells are islet cells.

35. *Ex vivo* cells ~~prepared by a process according to any one of claims 22~~ to 31

36. *Ex vivo* cells according to ~~claim~~ 35 wherein said cells are in a preparation that comprises an inhibitor or compound as defined in any one of claims 2, 4, 27 or ~~32~~.

37. *Ex vivo* cells according to claim 35 or claim 36, wherein the cells are genetically modified.

38 *Ex vivo* cells according to claim 35, 36 or 37 for use in a method of treatment of the human or animal body by therapy.

39. *Ex vivo* cells according to claim 38 which are islet cells for use in a method of treating diabetes.

40. *Ex vivo* cells according to claim 38 for use in a method of treating type I or type II diabetes, Alzheimer's disease, a spongiform encephalopathy, primary or secondary systemic amyloidosis, familial amyloidotic polyneuropathy, senile systemic amyloidosis, hereditary cerebral amyloid angiopathy, haemodialysis-related amyloidosis, Finnish hereditary amyloidosis, medullary carcinoma of the thyroid, atrial amyloidosis, lysozyme amyloidosis, or fibrinogen α-chain amyloidosis.

41. A pharmaceutical composition comprising a cell according to claim 35, 36 or 37 and a pharmaceutically acceptably carrier or diluent.

42. Use of an inhibitor as defined in any one of claims 2, 4, 22 or 27 in the manufacture of a medicament for inhibiting amyloid deposit formation by, or breaking amyloid deposits down in, a transplanted cell preparation.

43. A vessel for containing a culture of cells, which vessel is coated with an inhibitor or compound as defined in any one of claims 2, 4, 22 or 27.

44. A kit for culturing cells comprising a culture medium or culture medium pre-mix as defined in claim 32 or a vessel as defined in claim 43.

44. Use of an antibody that binds an inhibitor or compound as defined in claim 2, 4 or 27, or of a fragment of said antibody that retains the ability to bind the said inhibitor or compound, to identify a substance that can be used to prepare cells for transplantation in a process according to claim 22 or 23 .

46. Method of identifying an inhibitor that can be used to prepare cells for transplantation in a process according to claim 22 or 23, comprising contacting a

candidate substance with a mammalian cell and determining whether the candidate substance inhibits the formation of fibrils or causes the breakdown of fibrils, (i) the inhibition of formation of fibrils or (ii) the breakdown of fibrils. indicating that the substance is an inhibitor that can be used in said process.

47. Method of identifying an inhibitor that can be used to prepare cells for transplantation in a process according to claim 22 or 23, comprising contacting a candidate substance with a protein capable of forming fibrils, or with a fibril, and determining whether the substance inhibits the formation of the protein into a fibril, or whether the substance causes the breakdown of the fibril, (i) inhibition of fibril formation or, (ii) the breakdown of fibrils, indicating that the substance can be used in said process.

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48. A method according to claim 46 or 47 wherein the mammalian cell is any of the types of cells defined in claim 28, 29 or 31, or the fibrils comprise a protein as defined in claim 30 or 31.

49. A inhibitor identified by the use or method of any one of claims 45 to 48.

50. A process, culture medium, culture medium pre-mix, culture, *ex vivo* cells, pharmaceutical composition, use, vessel or kit according to any one of claims 22 to 44 wherein the inhibitor is an inhibitor as defined in claim 49.

51. Method of inhibiting fibril formation by, or breaking fibrils down in, a transplanted cell preparation comprising administering an inhibitor or compound as defined in any one of claims 2, 4, 22, 27 or 49 to a patient who has received a transplant of cells as defined in claim 35, 36 or 37.

52. Use of a compound as defined in any one of claims 1 to 5 in the manufacture of a medicament for inhibiting IAPP-associated amyloid deposits in a subject.